

WHAT IS CLAIMED IS:

1. A purified and isolated polypeptide having the primary structural conformation and biological properties of naturally-occurring metalloproteinase inhibitor.
2. A polypeptide according to Claim 1 wherein said polypeptide is the product of procaryotic or eucaryotic expression of an exogenous DNA sequence.
3. A polypeptide according to Claim 1 further characterized by being free of association with any mammalian protein.
4. A polypeptide according to Claim 2 wherein the exogenous DNA sequence is a cDNA sequence.
5. A polypeptide according to Claim 2 wherein the polypeptide is bovine metalloproteinase inhibitor.
6. A polypeptide according to Claim 2 wherein the exogenous DNA sequence is a genomic DNA sequence.
7. A polypeptide according to Claim 2 wherein the exogenous DNA sequence is carried on an autonomously replicating DNA plasmid or viral vector.
8. A polypeptide according to Claim 1 possessing part or all of the primary structural conformation of human metalloproteinase inhibitor as set forth in Figure 2 or any naturally occurring allelic variant thereof.

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9. A polypeptide according to Claim 1 which has the immunological properties of naturally-occurring metalloproteinase inhibitor.

5 10. A polypeptide according to Claim 1 which has the in vitro biological activity of naturally-occurring metalloproteinase inhibitor.

10 11. A polypeptide according to Claim 1 further characterized by being covalently associated with a detectable label substance.

15 12. A DNA sequence for use in securing expression in a procaryotic or eucaryotic host cell of a polypeptide product having at least a part of the primary structural conformation and one or more of the biological properties of naturally-occurring metalloproteinase inhibitor, said DNA sequence selected from among:

20 (a) the DNA sequence set out in Figure 1 or Figure 2 or their complementary strands;
(b) DNA sequences which hybridize to the DNA sequences defined in (a) or fragments thereof; and
(c) DNA sequences which, but for the
25 degeneracy of the genetic code, would hybridize to the DNA sequences defined in (a) and (b).

30 13. A procaryotic or eucaryotic host cell transformed or transfected with a DNA sequence according to Claim 12 in a manner allowing the host cell to express said polypeptide product.

35 14. A polypeptide product of the expression of a DNA sequence of Claim 12 in a procaryotic or eucaryotic host.

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15. A purified and isolated DNA sequence coding for procaryotic or eucaryotic host expression of a polypeptide having the primary structural conformation and biological properties of metalloproteinase inhibitor.
16. A cDNA sequence according to Claim 15.
17. A genomic DNA sequence according to Claim 15.
18. A DNA sequence according to Claim 15 wherein said DNA sequence codes for human metalloproteinase inhibitor.
19. A DNA sequence according to Claim 18 and including one or more codons preferred for expression in E. coli cells.
20. A DNA sequence according to Claim 15 having the sequence set out in Figure 2.
21. A DNA sequence according to Claim 15 and including one or more codons preferred for expression in yeast cells.
22. A DNA sequence according to Claim 15 covalently associated with a detectable label substance.
23. A DNA sequence coding for a polypeptide fragment or polypeptide analog of naturally-occurring metalloproteinase inhibitor.
24. A DNA sequence as in Claim 23 coding for methionyl metalloproteinase inhibitor.

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25. A biologically functional plasmid or viral DNA vector including a DNA sequence according to Claim 12.

5 26. A procaryotic or eucaryotic host cell stably transformed or transfected with a DNA vector according to Claim 25.

10 27. A polypeptide product of the expression in a procaryotic or eucaryotic host cell of a DNA sequence according to Claim 15.

15 28. A synthetic polypeptide having part or all of the amino acid sequence as set forth in Figure 2 and having one or more of the in vitro biological activities of naturally-occurring metalloproteinase inhibitor.

20 29. A synthetic polypeptide having part or all of the secondary conformation of part or all of the amino acid sequence set forth in Figure 2 and having a biological property of naturally-occurring human metalloproteinase inhibitor.

25 30. A process for the production of a polypeptide having part or all of the primary structural conformation and one or more of the biological properties of naturally occurring metalloproteinase inhibitor, said process comprising:

30 growing, under suitable nutrient conditions, procaryotic or eucaryotic host cells transformed or transfected with a DNA vector according to Claim 25, and isolating desired polypeptide products of the expression of DNA sequences in said vector.

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31. Purified and isolated human metalloproteinase inhibitor free of association with any human protein in glycosylated or nonglycosylated form.

5 32. A pharmaceutical composition comprising an effective amount of a polypeptide according to Claim 1 and a pharmaceutically acceptable diluent, adjuvant or carrier.

10 33. A method for inhibiting tumor cell dissemination in a mammal comprising administering an effective amount of a polypeptide according to Claim 1.

15 34. A method for treating rheumatoid arthritis in a mammal comprising administering an effective amount of a polypeptide according to Claim 1.

20 35. A DNA sequence coding for an analog of human metalloproteinase inhibitor selected from the group consisting of:
a) [Met⁻¹] metalloproteinase inhibitor; and
b) metalloproteinase inhibitor wherein one or more cysteines are replaced by alanine or serine.

25 36. A polypeptide product of the expression in a procaryotic or eucaryotic host cell of a DNA sequence according to Claim 35.

30 37. A preparation of MI which is greater than 95% pure and which comprises less than 0.5 ng of pyrogen per 0.5 mg of metalloproteinase inhibitor.

35 38. An antibody specifically binding metalloproteinase inhibitor.

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sub
a3

39. An antibody as in Claim 38 wherein said antibody is a monoclonal antibody.

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add
a4

add
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